Comments on Proposed Report on Carcinogens Listing of Diesel Exhaust Particulates

by

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for

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Board of Scientific Counselors
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I am Roger O. McClellan, President of the Chemical Industry of Toxicology, Research Triangle Park, NC. I am appearing before your subcommittee to offer my professional opinion on the classification of diesel exhaust particulates for inclusion in the report on carcinogens. The opinion I offer is based on my experience during the past 20 years conducting research and evaluating cell, whole animal, and epidemiological data relevant to assessing the human health risks of exposure to diesel exhaust particulates. That experience has included participation in review of diesel exhaust particulates conducted by the International Agency for Research on Cancer and the U.S. Environmental Protection Agency.

Numerous epidemiological investigations of occupational groups exposed to diesel exhaust have been conducted. The results of some studies have suggested a positive association of an increased risk of lung cancer with exposure to high levels of diesel exhaust. However, the results have not always been statistically significant. Reanalysis of the most substantial study (Garshick et al., 1988) by Crump et al., 1991 suggests that a high degree of caution should be exercised in interpreting the weak association originally reported by Garshick et al. The major limitations of the epidemiological studies are (a) a lack of control in many of the studies for confounding factors such as smoking, (2) the lack of measurements of exposure, and (3) the lack of any characterization data on the diesel exhaust particulates for exposures that occurred decades ago, (Nauss and the HEI Diesel Working Group, 1995). The latter two points are especially important because major improvements have occurred in diesel engine technology and diesel fuel quality over the past several decades. In my opinion, the epidemiological data support a conclusion of limited evidence of carcinogenicity for diesel exhaust particulates.

Numerous well-conducted studies, with rats and mice exposed chronically to varied levels of diesel exhaust have been conducted during the past two decades. The studies indicate that chronic high-level exposure of rats produces an increased incidence of lung cancer. Parallel studies in mice have been equivocal to clearly negative. It is now well established that the lung cancer in rats at high levels is a species specific effect associated with increased lung burdens of particulate matter, impaired clearance and chronic inflammation, i.e. a lung overload phenomena (McClellan, 1996). A meta-analysis of the groups of rats exposed to levels of particulate just below those producing lung overload did not identify any increase in lung cancer incidence. Numerous studies with extraordinarily high concentrations of organic solvent extracts of diesel exhaust particles have demonstrated mutagenic activity and an ability to cause skin cancer in mice. Taken in aggregate, the laboratory animal data, when interpreted for human relevance, supports a conclusion of limited evidence of carcinogenicity for diesel exhaust particulates.

Considering all of the data, it is my professional judgment that diesel exhaust particulates should be classified as "reasonably anticipated to be a human carcinogen" using the NTP criteria. In my opinion, if IARC were classifying diesel exhaust today using IARC criteria, diesel exhaust would be classified as "possibly carcinogenic to humans." I do not believe the weight of the evidence supports a classification of diesel exhaust particulate as a "human carcinogen."

References

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